

Exjade – treatment for iron overload

Information for patients and carers

What is Exjade (deferasirox)?

Exjade is an iron chelation medication. Chelation is a small molecule that binds iron and removes it from the body.

Why is too much body iron a bad thing?

Too much body iron is harmful to the tissues where it accumulates. Blood transfusion results in iron overload because each unit of blood contains iron as part of the haemoglobin in red blood cells.

The body has no natural way of removing all the extra iron so the iron is stored in cells. The liver is the main site for iron storage but once the liver is full of iron it will start to be deposited in other organs such as the hormone glands and the heart.

Liver complications

Although the liver is better equipped to deal with iron overload than some other tissues, poor control of liver iron will cause liver scarring and eventually liver failure (cirrhosis) – although this can take many years to develop. Liver cancer is a late complication. Removing iron from the liver reduces these risks.

Hormone problems

Iron can cause serious complications when it is deposited in the hormone glands. If iron is deposited in the pituitary gland which controls the hormones regulating growth and sexual development, young people may fail to enter puberty naturally. Older people may have difficulties conceiving because the hormones oestrogen (in women) and testosterone (in men) will stop being produced.

Other glands that are affected are the thyroid gland resulting in hypothyroidism, the pancreas resulting in diabetes, and the parathyroid gland resulting in low calcium levels in the blood. Unfortunately damage to the hormone glands is not reversible.

Heart problems

Iron can be deposited in the heart and, if severe levels are reached, can result in heart failure or abnormal heart rhythms (palpitations) which are both serious and can be life threatening. Heart failure is reversible with intensive chelation but it is completely avoidable if you follow treatment correctly.

The aim is to prevent problems developing in the first place. Therefore the best strategy for managing iron overload is avoiding high levels of iron. In general, liver iron values of above

7mg/g dry weight on a type of MRI called FerriScan liver iron assessment are the levels above which complications start to develop. We keep a liver iron target of below 5mg/g dry weight for our patients to ensure that iron overload complications do not develop.

All chelation drugs are effective if used appropriately and we will adjust chelation treatments so they are tolerable and fit in with your lifestyle as well as achieving the desired treatment goal.

When can Exjade be a useful treatment?

Exjade is designed to eliminate excess iron from the body. It can be used in children and adults who have iron overload as a result of blood transfusions. Exjade is also licensed for some other thalassaemia patients who develop too much body iron even without blood transfusion.

How does Exjade work?

Exjade is small enough to be absorbed through the gut and enter the blood stream. Binding of iron can occur in the blood stream or within tissues such as the liver or heart. Once iron is bound to Exjade, the iron complex is eliminated from the body through the bile and some in the faeces. Very little is eliminated in the urine so the urine does not go red as with other chelators that eliminate iron in the urine (desferal or deferiprone).

How is Exjade taken?

Exjade is available in tablet form. At the moment it is a dispersible tablet which is dropped into a glass of water to disperse (fall apart in small grains –it does not ‘dissolve’) before being swallowed. It needs to be mixed well in the glass with a wooden or plastic stirrer. The tablet can also be dispersed in a fruit drink such as apple or orange juice or squash. It should not be dispersed in fizzy drinks or drinks that are too thick (a smoothie or banana juice are too thick, for example). Exjade can be taken before or after food once a day. We recommend you take it at the same time each day.

How much should be taken and how often?

Exjade is taken once daily (seven days a week) and the dose needs to be adjusted from time to time in order to ensure effective chelation.

If the goal is to maintain a safe level of iron then we will normally use a dose of around 25-30 mg/kg/day. We may use doses of up to 40mg/kg/day if the goal is to reduce the total iron burden or if someone is on a very heavy transfusion programme. Sometimes, when iron is only accumulating slowly from exchange transfusion or in transfusion independent patients, doses as low as 10mg/kg/day are more appropriate.

It is very important to understand that an effective and safe dose depends on how much iron is already in the body and also on how rapidly iron is accumulating from blood transfusion or from iron absorption in the diet. If you are missing a couple of doses a week it will significantly reduce the impact of iron chelation and you could end up maintaining a high iron burden rather than reducing it.

It is also very important to understand that as the amount of iron falls with Exjade treatment, the dose needs to be decreased. If the doses given remain high when the iron level falls, there is a risk of 'over-chelation'. This could increase the risk of side effects from Exjade and that is why we monitor all patients on iron chelation carefully so doses can be adjusted from the ferritin trend.

Can Exjade be given with other iron chelators?

Exjade should be effective chelation therapy when given alone. So far clinical experience of combining Exjade with other chelators is fairly limited, although there are now some carefully conducted trials that show this can be useful and well tolerated. We will consider combination very rarely in those patients where iron burden is difficult to control.

Monitoring for effectiveness of Exjade

As with other chelators, the serum ferritin levels and trend is the most convenient way to monitor iron overload. An MRI scan of the liver and heart can be used for dose and regime adjustment and for risk assessment. These are typically performed about once a year.

How frequent are unwanted effects and what are they?

Like any drug, Exjade can have unwanted effects. These are more likely if the dose given is too high for the level of iron overload or the rate of iron loading. Fortunately the side effects of Exjade have been looked at in very large clinical trials so the frequency at which these occur are well known.

Effects on the gut

These occur in about 15 per cent of patients, are typically mild and do not persist. They include stomach pain, nausea, and vomiting, diarrhoea or constipation. These symptoms rarely require dose adjustment or stopping treatment and tend to settle down over a few weeks. If these persist or you suffer from severe vomiting or diarrhoea every time you take Exjade, the doctor prescribing the treatment should be informed.

Mostly these symptoms can be managed effectively by adjusting the time of day the medication is taken or taking it with food. Stomach ulcers have rarely occurred.

Skin rashes

These occur in about 11 per cent of patients. These are typically red and itchy and sometimes raised. They may occur all over the body or can be confined to the palms and feet. The rash typically develops within two weeks of starting treatment and responds well to temporary dose reduction. Sometimes steroids can be given for the rash, or very rarely permanent drug discontinuation is required.

Kidney function tests

Doctors monitor kidney function with a blood test called 'serum creatinine'. The serum creatinine increases by about 30 per cent in about one third of patients on Exjade and is not usually a cause for concern. However, in some cases Exjade may need to be interrupted or given at a lower dose.

Effects on the liver function tests

Usually liver function tests improve as body iron is decreased. Less than one per cent of patients may have an increase in liver enzymes greater than twice the upper limit of normal. In these cases, we may need to test the blood more frequently. If the liver enzymes rise more severely (more than five times the upper limit of normal) we may require interruption of treatment and occasionally permanent discontinuation.

Other effects

Rarely patients may develop cataracts.

Occasionally there have been reports of a problem known as metabolic acidosis occurring in patients who had pre-existing renal kidney problems or diarrhoea. We would consider interrupting Exjade in patients who develop metabolic acidosis.

Rarely patients have developed a severe allergic reaction known as anaphylaxis.

Monitoring for side effects of Exjade

It is important to monitor all patients on chelation treatment regularly to avoid under or over-treatment. There are some specific monitoring tests that need to be done for patients taking Exjade. These need to be done more often when the treatment is first started or if the dose is changed (particularly when the dose is increased).

- **Kidney function:** This should usually be monitored using the serum creatinine every time a sample is taken for a cross match (typically every three to four weeks).
- Urine protein can also be monitored at these visits
- **Liver function tests:** These should be done at the time of the cross match, at weekly intervals for four weeks after starting treatment and after a dose increase.
- **Eye and ear tests:** Ear tests are done about every one to two years. Eye tests are done when your doctor thinks it is necessary.

Contact details

Specialist nurses

Emma Prescott (nurse specialist, thalassaemia)	020 7288 5225
Matty Asante-Owusu (community matron, adults)	07920 711210
Edith Aimiuwu (nurse specialist, children)	07799 347161

Haematology consultants

Dr Bernard Davis
Dr Farrukh Shah
Dr Ali Rismani

Paediatric consultants

Dr Andrew Robins
Dr Sara Hamilton

If you or your family have any other questions please do not hesitate to contact any of the above healthcare professionals at Whittington Health.

Where can I get more information?

The UK Thalassaemia Society

19 The Broadway

London N14 6PH

Tel: 020 8882 0011

Website: www.ukts.org

The Sickle Cell Society

54 Station Rd, London NW10 4UA

Tel: 020 8861 7795

Website: <http://www.sicklecellsociety.org>

NHS 111

Tel: 111

www.nhs.uk/NHSEngland/AboutNHSservices/Emergencyandurgentcareservices/Pages/NHS-111.aspx

Patient advice and liaison service (PALS)

If you have a question, compliment, comment or concern please contact our PALS team on 020 7288 5551 or whh-tr.whitthealthPALS@nhs.net

If you need a large print, audio or translated copy of this leaflet please contact us on 020 7288 3081. We will try our best to meet your needs.

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